

Remarks

Claims 22-25, 34-37, 46 and 47 are pending in this application. Claims 22 and 36 have been amended without prejudice or disclaimer. No new matter has been added with these amendments. Applicants reserve the right to prosecute any cancelled or otherwise unclaimed subject matter in this or a separate application, as appropriate. Consideration and entry of these remarks and amendments is respectfully requested.

Amendments

Claims 22 and 26 have been amended to describe a method by which a body fluid sample is produced that is known to be depleted of antibodies reactive against particular MHC or HLA Class II molecules. These amendments are supported by the originally filed specification at, for example, paragraphs [016], [052], [057] -- [061]. As described therein, the claimed methods may be used to produce a product (e.g., a blood derived product) suitable for introduction into a recipient (e.g., who may be the same or a different person from whom the sample was obtained). It is of paramount importance that any such products be depleted of antibodies reactive in the recipient. Step c) of claims 22 and 36 provides a method for confirming that such products are, in fact, suitable for introduction into the recipient. As described below, the claimed methods are not described or in any way suggested by the cited art.

A. Rejections Under 35 U.S.C. § 103(a) over Hildebrand in view of Whitehead

Claims 22, 23, 25, 34-37, 46 and 47 stand rejected under 35 U.S.C. 103(a) as unpatentable over Hildebrand (US 2003/0166057) in view of Whitehead (U.S. Pat. No. 4,554,088) and Koll (US 2003/0125657). Applicants respectfully disagree and traverse these rejections as discussed below.

The Office Action alleged that Hildebrand teaches recombinant class II HLA molecules and that the same “can be used in methods for the removal of anti-HLA antibodies.” The Office Action also alleges that Koll discloses “the removal of anti-HLA antibodies from the blood of patients suffering from sensitization of HLA and cytotoxic anti-HLA antibodies (e.g., para 0016)... to provide treatment for the patients”. And Whitehead allegedly discloses “methods for depleting a sample of a biological molecule

of interest by contacting the sample with an immobilized bioaffinity absorbent (abstract col 2, col 6-8, 10 and 17).” Given these disclosures, the Office Action alleged that previously pending claims 22, 23, 25, 34-37, 46 and 47 would have been obvious to one of skill in the art. Applicants respectfully disagree and further believe that these rejections, if applied to the currently pending claims, would be improper.

On page 7, the Office Action alleged that Hildebrand “specifically suggested removal of anti-HLA antibodies from a sample”. Of the cited sections of Hildebrand, only paragraph [0120] refers to antibody removal, the reference stating that “purified, individual class I and class II MHC proteins would be highly useful” for “removal of anti-HLA antibodies from a patient.” At paragraph [0016] of Koll, the reference indicates that “[a]nti-human immunoglobulin coupled columns were used for the removal of immunoglobulin from the blood of human patients suffering from...sensitization to HLA.” However, other than Koll’s general indication that “anti-immunoglobulin coupled columns” may be useful, neither the Office Action nor the cited references explain how such procedures should actually be carried out. For example, none of the cited references suggest that Applicants’ claimed testing step should be included to confirm that antibodies to particular MHC / HLA Class II molecules *are in fact absent* from the treated body fluid sample. More specifically, none of the references (including Whitehead), teach Applicants’ step of testing the body fluid from which anti-MHC or anti-HLA antibodies may have been removed “by contacting the sample with a solid support comprising discrete sites, each site comprising recombinant HLA Class II molecules representing a specific, individual HLA Class II antigen, and detecting the binding or absence of binding of antibodies to the recombinant HLA Class II molecules at each site” such that it is known that particular antibodies have been removed. And it is only by including Applicants’ claimed testing step that the skilled artisan could introduce the treated body fluid sample to the recipient (e.g., who may be the same or a different person from whom the sample was obtained) knowing that the sample is suitable for that purpose.

The Office Action states that the “suggestion or motivation need not be expressly stated” in the cited references, and that “[t]he conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art

without any specific hint or suggestion in a particular reference.” However, as previously discussed, the U.S. Supreme Court has held that while an obviousness analysis “need not seek out precise teachings directed to the specific subject matter of the challenged claim”, “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”. KSR Int’l Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007) (citing In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006)). And this must be done without resorting to hindsight, as also pointed out by the Court in KSR:

A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning.” KSR Int’l Co. v. Teleflex Inc., 550 U.S. 398, 421 (2007), citing Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 36 (1966), (warning against a “temptation to read into the prior art the teachings of the invention in issue” and instructing courts to “guard against slipping into use of hindsight”)” (quoting Monroe Auto Equip. Co. v. Heckethorn Mfg. & Supply Co., 332 F.2d 406, 412 (CA6 1964))

There is simply no suggestion in any of the cited references to carry out Applicants’ instantly claimed methods. Applicants do not believe any “rational underpinning” for depleting a sample of MHC or HLA antibodies and testing that sample to confirm that particular MHC or HLA II antibodies have in fact been removed therefrom, as instantly claimed, can be drawn from the cited references in the absence of hindsight. As such, Applicants do not believe a *prima facie* case of obviousness can be made against the instantly pending claims. Applicants therefore respectfully request withdrawal of the pending rejections.

B. Rejections Under 35 U.S.C. § 103(a) over Whitehead in view of Viken and further in view of Lee (U.S. Pat. No. 6,150,122)

Claims 22, 23, 25, 34-37, 46 and 47 stand rejected under 35 U.S.C. 103(a) as unpatentable over Whitehead (U.S. Pat. No. 4,554,088) in view of Viken et al. (Human Immunology, Vol. 44, 1995, pp. 63-69) and further in view of Lee (U.S. Pat. No. 6,150,122). Applicants respectfully disagree and traverse these rejections as discussed below.

The Office Action alleged that Whitehead discloses a bioaffinity adsorbent that may be used to deplete a sample of a biological molecule. The Office Action admitted

that Whitehead does not teach a recombinant MHC Class II or HLA Class II molecule or an antibody thereto. This, the Office Action alleged, is taught by Vilken (“...the bioaffinity adsorbents can be recombinant HLA Class II molecules which bind specifically to antibodies of a sample (anti-HLA antibodies)”. And Lee is alleged to “disclose immobilized class II antigens for binding to the antibodies of the sample.” However, none of the cited references suggest that such testing should be conducted to confirm that antibodies to particular MHC / HLA Class II molecules are absent from the treated body fluid sample. None of the cited references teach Applicants’ step of testing the body fluid from which anti-MHC or anti-HLA antibodies may have been removed “by contacting the sample with a solid support comprising discrete sites, each site comprising recombinant HLA Class II molecules representing a specific, individual HLA Class II antigen, and detecting the binding or absence of binding of antibodies to the recombinant HLA Class II molecules at each site” such that it is known that particular antibodies have been removed. And it is only by doing so that the skilled artisan could confidently assure the patient that the treated body fluid sample is suitable for introduction into that patient.

The Office Action states that the “suggestion or motivation need not be expressly stated” in the cited references, and that “[t]he conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art without any specific hint or suggestion in a particular reference.” However, as previously discussed, the U.S. Supreme Court has held that while an obviousness analysis “need not seek out precise teachings directed to the specific subject matter of the challenged claim”, “there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”. KSR Int’l Co. v. Teleflex Inc., 127 S.Ct. 1727 (2007) (citing In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006)). And this must be done without resorting to hindsight, as also pointed out by the Court in KSR:

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into use of hindsight” (quoting *Monroe Auto Equip. Co. v. Heckethorn Mfg. & Supply Co.*, 332 F.2d 406, 412 (CA6 1964)))

There is simply no suggestion in any of the cited references to carry out Applicants’ instantly claimed methods. Applicants do not believe any “rational underpinning” for depleting a sample of MHC or HLA antibodies and testing that sample to confirm that particular MHC or HLA II antibodies have in fact been removed therefrom, as instantly claimed, can be drawn from the cited references in the absence of hindsight. There is simply no suggestion in any of the cited references to carry out Applicants’ instantly claimed methods. As such, Applicants do not believe a *prima facie* case of obviousness can be made against the instantly pending claims. Applicants therefore respectfully request withdrawal of the pending rejections.

Conclusions

Applicants believe that a full and complete Reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned. Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully Submitted,

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